REMARKS

The Present Invention

The present invention pertains to a process for the preparation of an intermediate useful for preparing kifunensine. The invention also relates to a process for preparing kifunensine.

The Pending Claims

Claims 1, 8-9, 11, 14-17, 19-23, and 24 are currently pending. Claims 1, 8-9, and 19-21 are directed to a process for preparing a compound of formula I. Claims 11-17 and 22-23 are directed to a process for preparing kifunensine. New claim 24 is directed to a process for preparing kifunensine.

Amendments to the Claims

Claims 12 and 13 have been canceled. Claim 24 has been added and is supported by the specification as filed at, for example, paragraphs [0019] and [0043]. No new matter has been added by way of these amendments.

Summary of the Office Action

Applicants note that the request for continued examination under 37 C.F.R. § 1.114 has been entered and that the finality of the previous Action has been withdrawn. Applicants also note that their submission of October 27, 2005, has been entered, but Applicants' submission of December 23, 2005, has not been considered. Applicants have re-submitted the Supplemental Preliminary Amendment and Declaration of Dr. Benjes dated December 12, 2005, with this reply for consideration.

Claims 12 and 13 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite on the ground that claims 12 and 13 improperly depend from claim 11 for failure to limit the scope of claim 11. Furthermore, claims 1, 8-9, 11-17, and 19-23 stand rejected as allegedly being unpatentable over Kayakiri et al. *Chem. Pharm. Bull.* **1991**, *39*, 1392-1396 ("Kayakiri I"), individually or in view of Kayakiri et al. *Tetrahedron Lett.* **1990**, *31*, 225-226 ("Kayakiri II"), in view of Morrison et al., *Org. Chem.* 3rd edition, (**1974**), 759. The Office asserts that Applicants merely change the sequential order of the reaction steps or combine steps/reagents from Kayakiri I and II, and that there is no indication of an interaction between the steps to suggest that such a combination could not be made. In addition, the Action asserts that one of ordinary skill would have known to use N-acetyl

protected D-mannosamine instead of an N-oxamoyl protected derivative. Further, the Action asserts that the specification lacks support for Applicants' claim that using the N-acetyl protecting group allows for large scale production. Reconsideration of the pending claims is respectfully requested.

Discussion of the Rejections

Solely in an effort to advance prosecution and not in acquiescence of the rejection, Applicants have canceled claims 12 and 13. In view of the foregoing, it is submitted that the indefiniteness rejection has been obviated and is now moot.

The rejection of claims 1, 8-9, 11-17, and 19-23 under 35 U.S.C. § 103(a) as allegedly being obvious in view of the Kayakiri references and Morrison et al., is respectfully traversed.

Applicants submit that using an N-acetyl protecting group in a process for preparing kifunensine is not disclosed in either Kayakiri I or II and that using an N-acetyl protecting group in a process for preparing kifunensine would not have been obvious to one skilled in the art in view of either Kayakiri I or II, in view of Morrison et al. Contrary to the assertion in the Office Action, neither Kayakiri I nor Kayakiri II teaches or suggests the use of an N-acetyl protecting group that is later cleaved, and neither Kayakiri I nor Kayakiri II teaches or even suggests the desirability of using an N-acetyl protecting group that would later be cleaved to allow for the formation of an oxamoyl group. Both Kayakiri I and Kayakiri II teach the oxamoylation step early in the process as an essential step of the process disclosed therein.

The Kayakiri references do not even suggest the use of protecting groups which are later cleaved. Instead, the Kayakiri references teach the use of N-oxalyl groups (i.e., moieties comprising N-C_2O_2-), more particularly, the N-ethyl oxalate (i.e., N-C_2O_2-OEt) and N-oxamoyl (i.e., N-C_2O_2-NH_2) groups as reactants which form the final molecule. In the Kayakiri references, N-ethyl oxalate and N-oxamoyl groups are introduced early in the process, and they are not cleaved during the process because they become part of the final product, kifunensine.

Moreover, when the teachings of Kayakiri et al. are followed, shortcomings of the Kayakiri methodology become apparent. For example, Applicants have observed irreproducibility in the silylation step and lower overall yields when attempting to replicate the work of Kayakiri. See Declaration of Benjes, paragraph 6 and Exhibit B, pages 1-2. See also the instant specification at, for example, paragraphs [0005], [0034], and [0053].

Applicants have discovered that using an N-acetyl protecting group, a protecting group which is introduced and then cleaved prior to the oxamoylation reaction, improves both the silylation reaction and overall yield of the process. See Declaration of Benjes, Exhibit B, pages 1-2.

Thus, Kayakiri et al. teach away from using the N-acetyl protecting group, a group which is introduced and then subsequently cleaved. Furthermore, the skilled artisan would not have a reasonable expectation of success in using an N-acetyl protecting group, given the harsh conditions necessary for its removal. See, e.g., Declaration of Benjes, paragraphs 6 and 7. One of ordinary skill in the art would not predict that the compound as a whole would survive such conditions, let alone improve the silylation reaction and overall yield.

Thus, the claimed processes are not disclosed in the cited references, and, in the absence of hindsight, Applicants submit that the skilled artisan would not have been motivated to modify the prior art with a reasonable expectation of success to obtain the claimed invention. The claimed processes lead to unexpected results when compared to the processes disclosed in the prior art, in particular, improvement in the silylation reaction and an increase in the overall yield of the reaction. Accordingly, Applicants submit that the obviousness rejection should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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